

Amendments to the Specification:

Please enter the attached sequence listing.

1. Please replace the paragraph on page 5 beginning on line 9 with the following amended paragraph:

The invention provides a method for attenuating virulence of CMV comprising functionally inactivating at least one open reading frame in a virulence region of a CMV genome having substantial identity to at least 300 bp, typically at least 500bp, of a 15 kb sequence present in the genome of the AD169 strain of CMV and/or absent from the genome of highly-passaged Towne (i.e., more than 50-100 passages). In an aspect, the method functionally inactivates at least one open reading frame present in a genomic region of a CMV genome having substantial identity to at least 300bp of a 13 kb sequence present in the genome of the Toledo strain of CMV and absent from the genome of the Towne strain of CMV. In an embodiment, the method functionally inactivates at least one open reading frame present in a genomic region of a CMV genome having substantial identity to at least 500bp of the sequence shown in Figs. 1A through [1T] 1R (SEQ ID NO:1). In an embodiment, the method functionally inactivates at least the open reading frame corresponding to UL 148 as identified herein. In a variation, the method ~~functionally~~ functionally inactivates open reading frames in the region spanning UL138 to UL 148. In an embodiment, the method functionally inactivates UL138, UL139, UL140, UL141, UL 142, UL 143, UL144, UL145, UL146, UL147, and/or UL148. In a variation, UL148 is inactivated singly or in combination with other open reading frames of the Toledo genomic region. In a specific embodiment, UL148 is inactivated in combination with UL141 and/or UL144. Typically, such Toledo region-attenuated CMV variants comprise at least 500bp of the Toledo genomic region or a homolog region having at least 80 percent sequence identity; frequently they comprise at least 1.0 kbp of the Toledo genomic region or homolog virulence region; often they contain at least 5.0 kbp to 8.0 kbp of the Toledo genomic region or homolog virulence region, and can comprise up to a complete Toledo genomic region or homolog virulence region. It is possible for a synthetic virulence region to be comprised of portions of two or more virulence regions (e.g., such as a chimeric virulence region

comprising part of the Toledo genomic region from a first clinical isolate with a complementing portion of the Toledo genomic region of a second clinical isolate).

2. Please replace the paragraph on page 14 beginning on line 2 with the following amended paragraph:

Figures 1A-1R. Nucleotide sequence of Toledo genome region isolated from Toledo strain of HCMV (SEQ ID NO:1).

3. Please replace the paragraph on page 14 beginning on line 4 with the following amended paragraph:

Figures 2A-2H . Deduced amino acid sequences of open reading frames UL130, and UL132 through UL151 (SEQ ID NOs:2-27, respectively). ~~Convnetional~~ Conventional single letter abbreviations are used.

4. Please replace the paragraph on page 17 beginning on line 8 with the following amended paragraph:

The following terms are used to describe the sequence relationships between two or more polynucleotides: "reference sequence", "comparison window", "sequence identity", "percentage of sequence identity", and "substantial identity". A "reference sequence" is a defined sequence used as a basis for a sequence comparison; a reference sequence may be a subset of a larger sequence, for example, as a segment of a full-length cDNA or gene sequence given in a sequence listing, such as a polynucleotide sequence of Fig. 1A-1R (SEQ ID NO. 1), or may comprise a complete cDNA or gene sequence. A full-length cDNA or gene sequence is defined as a polynucleotide containing the sequence(s) necessary to encode a complete protein product, including a translation initiation codon and a translation termination codon, unless linked to another encoding sequence in a format for production as a fusion protein. Generally, a reference sequence is at least 20 nucleotides in length, frequently at least 25 nucleotides in length, and often at least 50 nucleotides in length. Since two polynucotides may each (1) comprise a sequence (i.e., a portion of the complete polynucleotide sequence) that is similar between the two polynucleotides, and (2) may

further comprise a sequence that is divergent between the two polynucleotides, sequence comparisons between two (or more) polynucleotides are typically performed by comparing sequences of the two polynucleotides over a "comparison window" to identify and compare local regions of sequence similarity.

5. Please replace the paragraph on page 27 beginning on line 19 with the following amended paragraph:

Figures 1A-1R show the nucleotide sequence of Toledo genome region isolated from Toledo strain of HCMV (SEQ ID NO. 1). Figures 2A-2H show the deduced amino acid sequences of open reading frames UL130, and UL132 through UL151 (SEQ ID NOs 2-27, respectively).

6. Please replace the paragraph on page 28 beginning on line 28 (through page 29, line 19) with the following amended paragraph:

The invention provides a method for attenuating virulence of CMV comprising functionally inactivating at least one open reading frame in a genomic region of a CMV genome having substantial identity to at least 300 bp, typically at least 500bp, of an approximately 15 kb sequence present in the genome of the Toledo strain of CMV and absent from the genome of the AD169 strain of CMV. In an aspect, the method functionally inactivates at least one open reading frame present in a genomic region of a CMV genome having substantial identity to at least 300bp of a 13 kb sequence present in the genome of the Toledo strain of CMV and absent from the genome of the highly-passaged Towne strain of CMV. In an embodiment, the method functionally inactivates at least one open reading frame present in a genomic region of a CMV genome having substantial identity to at least 500bp of the sequence shown in Figs. 1A through ~~[[1T]]~~ 1R (SEQ ID NO:1). In an embodiment, the method functionally inactivates at least the open reading frame corresponding to UL 148 as identified herein. In a variation, the method ~~functionally~~ functionally inactivates open reading frames in the region spanning UL138 to UL 148. In an embodiment, the method functionally inactivates UL138, UL139, UL140, UL141, UL 142, UL 143, UL144, UL145, UL146, UL147, and/or UL148. In a variation, UL148 is inactivated singly or in combination with other open reading frames of the Toledo genomic

region. In a specific embodiment, UL148 is inactivated in combination with UL141 and/or UL144. Inactivation is typically accomplished by genetic engineering and involves predetermined mutations (which may include additions, transpositions, or deletions), generally of the specific type which are not known to occur naturally in CMV strains even after extensive passaging.